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ABOUT COVER

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OPINION REVIEW

How to construct neuroscience-informed psychiatric classification? Towards nomothetic networks psychiatry

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Abstract

Psychiatry remains in a permanent state of crisis, which fragmented psychiatry from the field of medicine. The crisis in psychiatry is evidenced by the many different competing approaches to psychiatric illness including psychodynamic, biological, molecular, pan-omics, precision, cognitive and phenomenological psychiatry, folk psychology, mind-brain dualism, descriptive psychopathology, and postpsychiatry. The current "gold standard" Diagnostic and Statistical Manual of Mental Disorders/International Classification of Diseases taxonomies of mood disorders and schizophrenia are unreliable and preclude to employ a deductive reasoning approach. Therefore, it is not surprising that mood disorders and schizophrenia research was unable to revise the conventional classifications and did not provide more adequate therapeutic approaches. The aim of this paper is to explain the new nomothetic network psychiatry (NNP) approach, which uses machine learning methods to build data-driven causal models of mental illness by assembling risk-resilience, adverse outcome pathways (AOP), cognitome, brainome, staging, symptomatome, and phenomenome latent scores in a causal model. The latter may be trained, tested and validated with Partial Least Squares analysis. This approach not only allows to compute pathway-phenotypes or biosignatures, but also to construct reliable and replicable nomothetic networks, which are, therefore, generalizable as disease models. After integrating the validated feature vectors into a well-fitting nomothetic network, clustering analysis may be applied on the latent variable scores of the R/R, AOP, cognitome, brainome, and phenome latent vectors. This pattern recognition method may expose new (transdiagnostic) classes of patients which if cross-validated in independent samples may constitute new (transdiagnostic) nosological categories.

Key Words: Psychiatry; Major depression; Mood disorders; Schizophrenia; Antioxidants; Oxydative stress

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Core Tip: The nomothetic network psychiatry approach is a new method which aims to construct causal models of schizophrenia and mood disorders by integrating all features of those mental illnesses into a data-driven model. These features comprise data on risk-resilience, adverse outcome pathways, the cognitome, brainome, symptomatome, staging, and the phenomenome. Partial Least Squares analysis may be employed to train, test, and validate those models and to build pathway-phenotypes or biosignatures. Clustering analysis performed on all illness features, reduced into latent traits scores, may expose relevant new transdiagnostic classes.

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INTRODUCTION

For the past 200 years, psychiatry remained a discipline plagued by conceptual controversies, whose roots go back to its poor ontological and epistemological foundations[1]. Psychiatry remained in a permanent state of crisis due to methodological mistrust in psychiatric case definitions, which fragmented psychiatry from the field of medicine[2]. The crisis is psychiatry is further evidenced by the many different competing approaches and ways to understand mental and psychiatric disorders including the etiological approach of psychodynamic psychiatry, biological, molecular, pan-omics, and precision psychiatry, cognitive psychiatry, folk psychology, the mind-brain dualism, descriptive psychopathology, postpsychiatry, and phenomenological psychiatry. Moreover, the gold standard taxonomies used to diagnose mood disorders and schizophrenia are not reliable[3,4].

Recently, we employed a new approach, namely the nomothetic network psychiatry (NNP) approach, which uses machine learning methods to build new data-driven models of mood disorders and schizophrenia using all features of those disorders including etiological, context centered hermeneutic, biological, molecular, cognitive, descriptive psychopathological, and phenomenological features[3-7]. The aim of this opinion paper is to review how to build nomothetic networks using Partial least Squares (PLS) analysis and how to expose new classifications of these disorders using unsupervised pattern recognition techniques.

FOLK PSYCHOLOGY

Folk or commonsense psychology tries to explain the mental state of individuals including symptoms, cognitions, or behaviors as the outcome of everyday life psychology and daily life experiences such as pleasure, sensations, pain, common beliefs, perceptions, *etc*.[8]. Folk psychology narratives are embodied in psychiatric inventories, either observational interviews or self-evaluation scales, which are supposed to deliver meaningful information intended to contribute to the diagnostic criteria of the conventional psychiatric classification systems or to rating scales that measure severity of illness. Thus, structural components of current psychiatric inventories are decomposed into items (statements and questions) some of which are formulated in a folk psychology-like language. For example, items such as "I cry easily" or "I feel down and depressed" are borrowed from folk psychology. In a futile effort to translate these symptoms into a more technical and medical jargon, such as depressive mood for instance (anhedonia and dysthymia), those items are then scored on a 4- or 7-degrees Likert scale so that the total score may resemble a statistically digestible entity. In this manner, common sense folk psychology expressions are converted into "diagnostic" statements without any reference to independent validators. The most common "state" dependent clinical measures or inventories in psychiatry remain folk psychology narratives with some window dressing for

statistical purposes. What is missing in such perspective is the biological, neuronal, and cognitive basis to better understand the existing phenomena in psychopathology, which is declared on the agenda of post-modern psychiatry.

MIND-BRAIN AND MIND-BODY DUALISM

There are two main intellectual frameworks which outline the rationale behind the scientific enterprise in psychiatry. The first is psycho-physical dualism which is supposed to drive the advances in psychotherapy and psychosocial interventions in mental illness. Mind-body dualism is the theory which proposes that mental phenomena are non-physical or that not all mental processes are physical. As such, mind and body would be, at least in part, separable entities[9,10]. The common psychiatric approach is essentially focused on what might be described as "mind" in terms of the mind-brain debate.

The second is the physicalism stance, which considers that everything is physical[11]. Physicalism and materialism are implicated as a primary assumption in influential advances in psychiatric research including biological, molecular, and pan-omics psychiatry, functional neuroimaging, and cognitive science[12].

LOCALIZATIONISM AND DYNAMIC PSYCHIATRY

Early efforts initiated by the Wilhelm Griesinger and the Wernicke-Kleist-Leonhard schools tried to consolidate psychiatric nosology using organic etiological factors[13]. These early theories, associated with the notions of localizationism, culminated in the works of Karl Wernicke and Karl Kleist and Maynert-Wernicke's connectionism. Psychodynamic theories, initiated by Sigmund Freud, and later versions of psychoanalysis, applied a conceptual organization of psychiatric syndromes based on a psychodynamic etiologic approach but remained grounded on the tacit assumptions of psychophysical dualism. However, attempts to bring together the disparate etiological explanatory models of psychodynamic paradigms and localizationism and clinical diagnoses proved to be inefficient. Neither of those views offered consolidated and sustainable pictures of psychiatric diagnoses applicable in the medical practice.

DESCRIPTIVE AND PHENOMENOLOGICAL PSYCHIATRY

Descriptive psychopathology or psychiatry focusses on readily observable behaviors and symptoms, rather than on underlying psychoanalytic or organic etiologies. Phenomenological psychopathology focuses on the patients subjective, own lived experiences of selfhood, space, time, body, and mind[14].

Current gold standard psychiatric classifications are based on descriptive and phenomenological psychopathology, including the Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification of Diseases (ICD) taxonomies. These case definitions are derived from cross-culturally diverse, even sometimes unique criteria[15], established *ex convention* by professional bodies like the American Psychiatric Association (APA) and the World Health Association (WHO). These *ex consensus-based* case definitions of nosological psychiatric classes use de-contextualized narratives and descriptive features of the disorder derived from folk psychology-like self-reports by the patient and observer-based interviews[16].

Due to the missing etiological and biomarker foundations, one crucial limitation of the current classifications, such as DSM-5 and ICD-10, is their top-down manner of generation[3-5,16]. The structured interviews, which are used to construct diagnostic categories, pre-define the clinical diagnosis before other tests are performed, including etiologic, state and trait-biomarkers, brain imaging, and cognitive probes. In that regard the diagnosis remains based on controversial and value laden statements, whereas the causal and biological measures are supposed to be concomitant data, either supporting the diagnosis or not. However, no falsification or dispute of the diagnostic assumption is possible based on information from outside the data source of the clinical interview, thus precluding a top-down deductive approach[3-5]. It should be added that those professional bodies are most often under the influence of para-motivation from the pharmaceutical industry or other confounds which leads to deeply controversial and in the end of the day counter-productive debates on the

existence of specific case definitions of psychiatric illness.

Moreover, the taxonomies used to make the diagnosis of psychotic disorders show inadequate reliability validity as for example indicated by significant differences in the diagnoses of DSM-III-R, DSM-IV, ICD-8, ICD-9, and ICD-10 classifications[16,17]. There is considerable inter-departmental diagnostic variability in the ICD-8 and ICD-10 diagnosis[18] explaining that schizophrenia may be often overdiagnosed or underdiagnosed[17]. In addition, the DSM suffers from a poor demarcation of the clinical heterogeneity present in schizophrenia[4,19]. For example, using machine learning techniques we discovered that schizophrenia consists of qualitatively distinct categories (including deficit *vs* non-deficit schizophrenia)[20], indicating that schizophrenia biomarker research which does not take this distinction into account is bound to fail. Also, the DSM case definitions of mood disorders including major depressive disorder (MDD) lack reliability validity[21], with MDD taxonomies showing minimal agreement between psychiatrists[22]. Furthermore, there was limited or no unification and harmonization of the DSM case definitions[18]. All in all, these taxonomies lack reliability and validity and are therefore counterproductive for research purposes[3-5,16,23-25].

BIOLOGICAL, MOLECULAR AND COGNITIVE PSYCHIATRY

A more radical physicalism theory, namely eliminative materialism, has been outlined in the past decades, especially under the influence of Churchland[26]. This theory applied to psychiatry relies on neuroscience and aims to replace the "folk" psychology vocabulary and methods on a systematic level by material concepts, namely aberrations in brain functions and neurocircuitry. Biological psychiatry aims to explain mental illness in terms of biological aberrations in neuronal functions; molecular psychiatry explains mental illness based on molecular pathways including the effects of genes and intracellular networks; and cognitive psychiatry explains mental illness though effects of cognitive impairments and their neuronal substrates. Nevertheless, the biological, molecular and cognitive approaches turned out to be insufficient to delineate biomarker or cognitive tools that externally validate the case definitions.

Biological, molecular and cognitive psychiatry research generally uses the "gold standard" DSM/ICD case definitions of mood and psychotic disorders in top-down research[3,4,16]. These methods commonly enter diagnosis as explanatory variable in GLM analysis or analysis of variance to analyze alterations in causome (*e.g.*, early lifetime trauma), biomarker levels, brainome data, and cognitive probe scores. The latter are entered as the dependent variables even when causal reasoning shows that they should be employed as the explanatory variables in logistic regression or other machine learning techniques, including neural networks. Consequently, most biological and cognitive psychiatry research projects employ unreliable diagnostic classes applied in inadequate model assumptions and tested with inappropriate statistical tests[3-5]. Also, molecular psychiatry uses a similar approach when examining pathways and networks or when conducting studies which associate genetic markers with the DSM/ICD taxonomies. A newer method, namely the Research Diagnostic criteria (RDoC), developed by the NIH, tries to integrate genetic, neurodevelopmental, environmental factors, with social, regulatory, cognitive and social domains, with negative and positive valence[25]. However, also the RDoC is largely a top-down concept driven by ex-consensus commitments by experts.

Another critical point is that the entire hypostasis of eliminative materialism of biological, molecular, and cognitive psychiatry is a fragmented or *"patchy" reductionist* approach[27] whereby psychiatric diagnoses tend to be reduced to neuronal entities, genetic markers, plasma biomarkers, intracellular signaling molecules, or functional MRI responses to emotional tasks. What is missing is an integrated model with precise mapping of genomics data, specific (causal and protective) and generalized (*e.g.*, context centered and lifestyle) environmental factors, and phenome features. All in all, the current "gold standard" DSM/ICD taxonomies are unreliable constructs and preclude using a deductive reasoning approach and, therefore, it is not surprising that biological, molecular, and cognitive psychiatry research was unable to revise the conventional classifications and did not provide valid predictions from a therapeutic perspective.

PAN-OMICS AND PRECISION PSYCHIATRY

Pan-omics psychiatry proposes to use systems biomedicine to decipher the complex non-linear interactions between pathways and intracellular networks that govern those pathways, and the multifactorial factors including genes and environmental factors that may trigger those pathways/networks[28]. Pan-omics psychiatry proposes to use a data-driven bottom-up approach to compute biosignatures consisting of molecular pathways and networks and symptoms as well as environmental features thereby developing pathway-phenotypes[28,29]. A related field is precision psychiatry, which is based on precision medicine defined as "an emerging approach for treatment and prevention that takes into account each person's variability in genes, environment, and lifestyle"[30]. Precision psychiatry aims to transform the psychiatric landscape through a bottom-up approach applied to pan-omics using system biology and computer science to compute a biosignature, which in turn may be used in a top-down approach to help to understand domains, which differ from components but allow to construct endophenotypes[31]. Both pan-omics and precision psychiatry propose to combine cognitive neuroscience, neural circuits, big data, molecular biosignatures, individual characteristics, physiology, and environment into a biosignature, which is a feature set defining an endophenotype[28,31]. These methods[31], however, do not aim to integrate all features of complex psychiatric disorders into a model characterized by causal paths linking causome (all possible causal factors), protectome (all possible protective factors), adverse output pathways (AOPs, namely biological, molecular, pan-omics, brain imaging features) and phenome (cognitome, symptomatome and phenomenome) feature sets.

BUILDING BLOCKS OF AN INTEGRATED MODEL

Figure 1 shows a causal theoretical model applicable to mood and psychotic disorders[3-7]. Causal reasoning based on state-of-the-art knowledge of these mental disorders indicates that causome features including genes and its products including enzymatic activity as well as specific environmentome factors (*e.g.*, early lifetime trauma) predict AOPs and the phenome of the illness[32]. Moreover, the generalized environmentome (including lifestyle, nutrition, toxins, context centered social, cultural, and political factors) should be added. Pan-omics may be employed to measure causome (genomics) and AOPs (*e.g.*, immunomics, epigenomics, transcriptomics, metabolomics, and proteomics). In psychiatry, another important AOP component is the brainome, which may be assessed using in vivo histology spectroscopy and magnetic resonance imaging. Also, the phenome of psychiatric disorders is very complex and consists of various feature sets including (1) staging of the disorder, as defined by recurrence of episodes and suicidal attempts, chronicity, *etc*.[32]; (2) the cognitome, namely the aggregate of cognitive features of the illness including in memory, executive functions, and attention; (3) the symptomatome, namely the aggregate of observed clinical symptoms, illness severity, subtypes, treatment responsivity; and (4) the phenomenome, namely the illness features as experienced by the patient[3,4].

One of the aims of our new nomothetic network psychiatry (NNP) approach is to reunify such data (1, 2, 3 and 4) into an illness model, which integrates different approaches including etiological, biological, molecular, pan-omics, cognitive, descriptive and phenomenological psychiatry, as well as folk psychology and postpsychiatry. In fact, machine learning conducted on these data will extract and select the most important features in a process referred to as feature re-engineering, selection, and learning to make the most accurate models of mood and psychotic disorders.

THE PRE-SPECIFIED CAUSAL FRAMEWORK

Figure 2 shows a framework or general structure which is based on scientific evidence linking a multitude of causome, protectome, AOPs, cognitome, brainome, staging, symptomatome, and phenomenome data. The selection of variables (indicators) and the concept of the framework are guided by the available theoretical knowledge, expertise, and information accumulated over the past decades and by formal causal reasoning. Nevertheless, the framework shown in Figure 2 is far for complete as for example socio-demographic data and generalized environmentome factors (*e.g.*, those

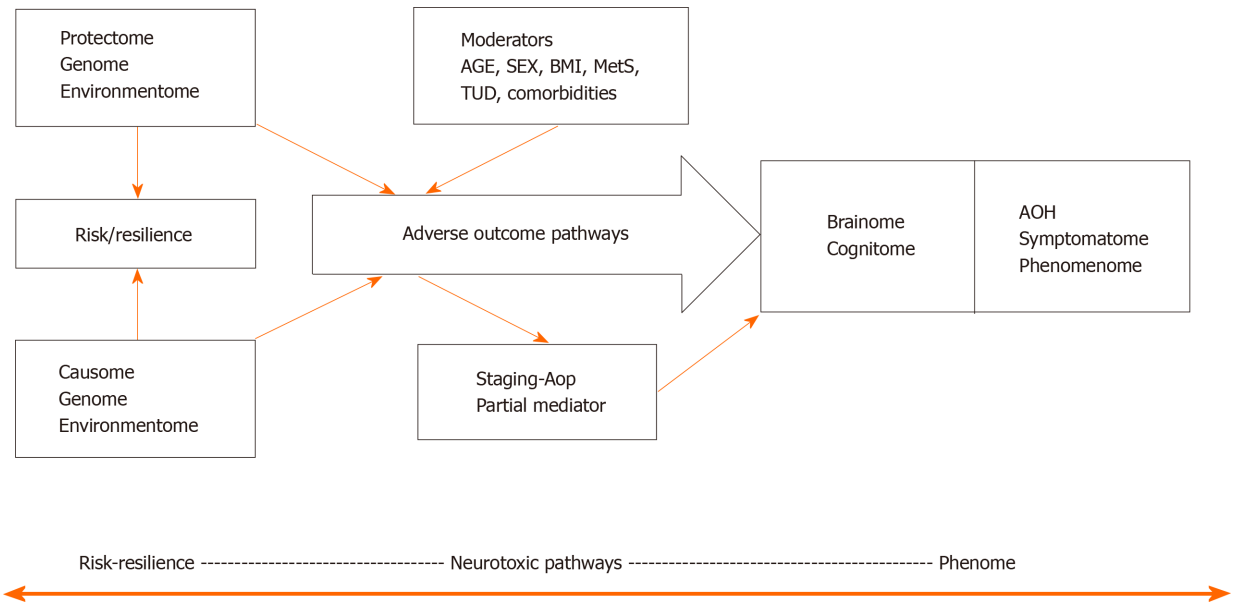

Figure 1 A causal theoretical model applicable to mood and psychotic disorders. This model links causome features (genes and gene products and environmentome factors) with adverse outcome pathways (AOP) and the phenome of the illness. The phenome consists of brainome and cognitome factors and adverse health outcomes including in the symptomatome and the phenomenome. Moreover, staging of illness may partly mediate the effects of risk/resilience and AOPs on the phenome. Age, sex, body mass index, metabolic syndrome, tobacco use disorder, and psychiatric and medical comorbidities are frequent moderators of the effects of R/R and AOPs on the phenome. AOP: Adverse outcome pathway; AOH: Adverse health outcome; MetS: Metabolic syndrome; BMI: Body mass index.

relevant to postpsychiatry) should be added to the model but are deleted from the figure for reasons of clarity. Consequently, data (facts) are accumulated to test this theoretical framework[33].

The multitude of data to be entered should first be reduced (dimensionality reduction) to a smaller number of relevant feature sets or vectors using feature construction processes[3,4]. The first step is to re-engineer the causome and protectome data into one of more new feature sets reflecting risk-resilience (R/R), namely the balance between causal and risk factors[3,4]. These R/R feature sets can consequently be used as input variables (predictors) in logistic models, regression analysis, and neural networks to expose their effects on the downstream features of the framework (AOP and phenome data). For example, in schizophrenia, we established that R/R indices re-engineered from genome data, *i.e.*, paraoxonase 1 (PON1) Q192R genotype combined with PON1 enzymatic activity, zonulin levels (a product of the haptoglobin 2-2 genotype), and lowered natural IgM (a protectome factor) predict AOPs (neuro-immune and neuro-oxidative toxicity pathways), cognitome (episodic and semantic memory and executive functions), symptomatome (psychosis, hostility, excitation, mannerism, negative symptoms) and phenomenome (self-rated quality of life) features[4]. In mood disorders, a new R/R index consisting of the PON1 Q192R genotype combined with PON1 enzymatic activity and early lifetime trauma predicts AOPs (antioxidant defenses and neuro-oxidative stress biomarkers), the symptomatome (depression severity, suicidal ideation, and mood disorders subtypes such as treatment resistance and melancholia) and the phenomenome (self-rated quality of life and disabilities)[3].

In the framework displayed in Figure 2, the newly re-engineered R/R feature sets are entered as input variables and can predict downstream feature sets as delineated through formal causal reasoning. The indicators of all downstream concepts are represented as latent vectors extracted from a set of features in reflective models because the aim is to construct a single underlying trait (*e.g.*, the symptomatome) which explains its manifestations (*e.g.*, all different symptom domains and phenotypes)[3-7]. The phenome feature sets are entered as output variables, whereas AOPs, cognitomone, and brainome feature sets predict the phenome and are predicted by the R/R features. It should be underscored that this method allows to reduce many features into a few relevant single traits. As such, the framework displayed in Figure 2 comprises one dependent variable (namely a latent vector reflecting the phenomenome) which is predicted by seven input variables, namely the RR, AOP, brainome, and symptomatome latent vectors. This parsimonious formal causal framework can then be trained, tested and validated using PLS structural equation

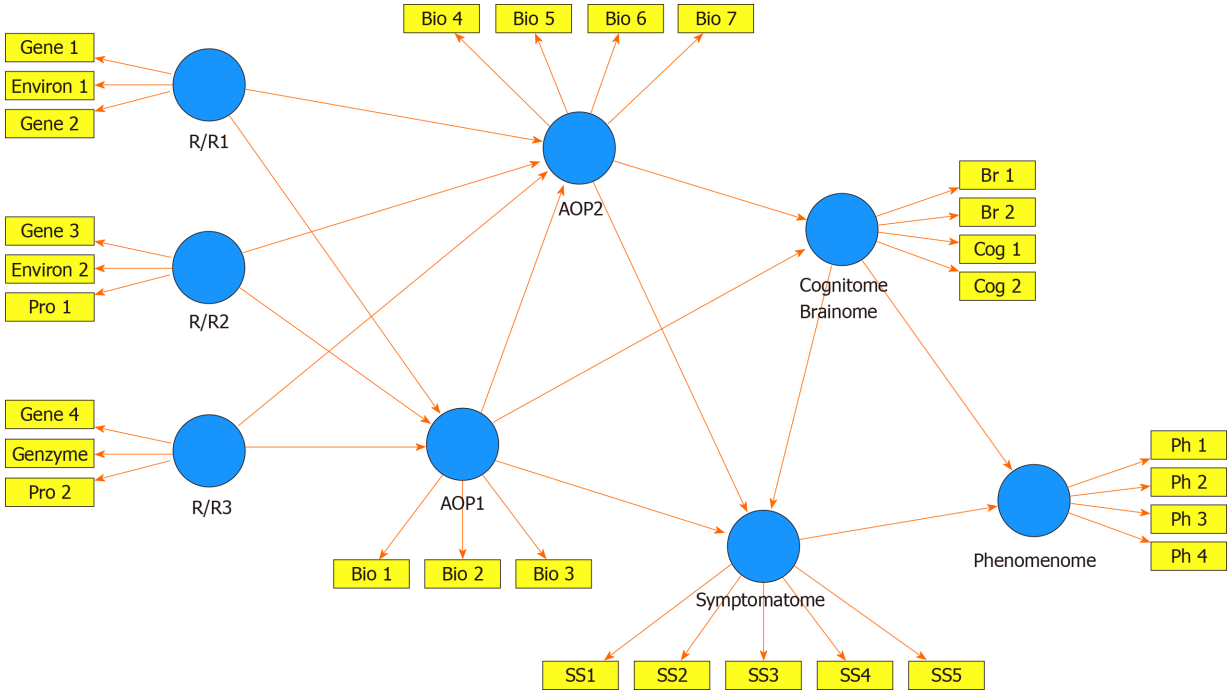

Figure 2 A causal framework of mental illness. This framework links a multitude of risk/resilience (R/R) features, with adverse outcome pathways (AOPs), the cognitome and brainome, the symptomatome, and phenomenome of mood disorders and schizophrenia. The R/R features are computed as a combination of causal and protective (Pro) genetic and environmental (Environ) features. The AOP feature sets are latent vectors (in reflective models) extracted from molecular or biological pathways/networks (Bio). The cognitome-brainome feature set is a latent vector extracted from cognitive test probe scores (Cog) and brain imaging (Br) scores. The symptomatome is entered as a latent vector extracted from symptom profiles, staging, and phenotypes (SS). The phenomenome is entered as a latent vector extracted from phenomenological data. R/R: Risk/resilience; AOP: Adverse outcome pathway; Pro: Protective; Bio: Biological; SS: Symptom profiles, staging, and phenotypes; Br: Brain imaging; Cog: Cognitive test probe scores.

modeling[3-7,34].

FROM A CAUSAL FRAMEWORK TO A CAUSALLY MODELED NOMOTHETIC NETWORK

PLS analysis allows to build pathway-phenotypes or biosignatures and train and evaluate a novel nomothetic model based on a combination of factor and regression analysis. Pathway-phenotypes may be exposed by combining for example AOPs with cognitome features into new reflective indicators of molecular paths and cognitive functions that underpin the illness[35]. Causal-pathway-phenotypes may be exposed by combining causome (*e.g.*, number of transfusions in transfusion-dependent thalassemia or TDT), AOPs (iron overload biomarkers and neuro-immune pathways as a consequence of the transfusions) with the phenome (depressive symptoms) into reflective indicators of a single latent trait, namely "depression due to immune activation as a consequence of transfusions and iron overload in TDT"[7]. Interestingly, in mood disorders, but not schizophrenia, symptomatome and phenomenome features may be combined as reflective manifestations of a single latent trait, namely the clinical – phenomenological phenome[3,4].

Figure 3 shows that the theoretical framework including new pathway-phenotypes can be trained and tested employing PLS on bootstrapped samples (*e.g.*, 5.000)[36]. Goodness of fit should be assessed using standardized root mean square residuals to avoid model misspecifications. The validity reliability of the latent vectors should be evaluated using psychometric properties such as composite reliability, rho-A, Cronbach's alpha, and average variance extracted values. All indicators of the LVs should show adequate loadings > 0.5 or by preference > 0.66[36]. Moreover, confirmatory tetrad analysis (CTA) should be used to ascertain whether the LV models are not mis-specified as reflective models, and blindfolding is used to test the construct cross-validated redundancies, which test the predictive relevance of the output LVs in the model[3,4]. Sample size determination and statistical power estimation should be performed based on (1) the psychometric properties of the vectors (factor loadings)

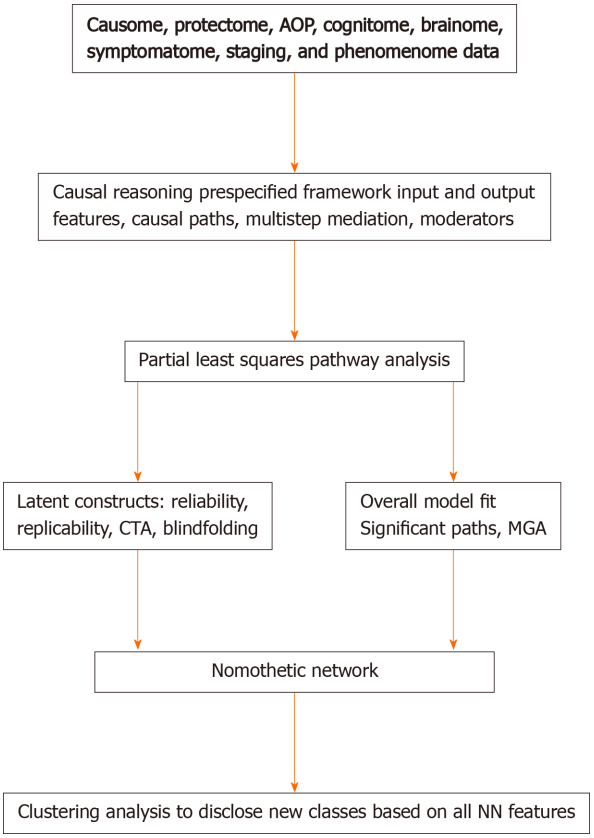

Figure 3 Nomothetic Network Psychiatry. Use of Partial Least Squares analysis to construct nomothetic networks (NN). Clustering techniques are conducted on the latent variable scores to expose new diagnostic classes. PLS: Partial Least Squares; NN: Nomothetic networks; AOP: Adverse outcome pathways; CTA: Confirmatory tetrad analysis; MGA: Multi-group analysis.

and the strength of the intercorrelations among the vectors, (2) the explained variance and the maximum number of arrows pointing to a construct, or (3) power analysis specific to multiple regression analysis[37,38]. These methods show that to achieve a power of 0.8 in the PLS model displayed in Maes *et al*[3] a relatively small sample size of n = 70-127 is sufficient. Nevertheless, larger sample sizes will yield more stable parameter estimates.

Consequently, PLS is conducted on bootstrapped samples which expose the path coefficients with exact p-values of all significant links (paths), as well as the total direct and indirect and specific indirect effects. Importantly, the indirect effects indicate the mediating effects of upstream on downstream indicators including in multistep mediating models. For example, in Figure 2, the R/R feature sets may have significant indirect effects on the phenomenome, which are mediated by the paths from AOP1 to the symptomatome or by the path from AOP2 to the cognitome to the symptomatome. In addition, also moderator (interaction) effects between 2 or more downstream indicators on upstream indicators may be added to the model which may account for possible moderating effects of age, sex, metabolic syndrome, and comorbidities. Finally, PLS allows to establish possible group differences in the model or paths using Multi-Group-Analysis (PLS-MGA) or permutations, which can be employed to examine differences in the model or paths, for example between different genotypes and between men and women. The latter is important to examine in schizophrenia and mood disorders because sexual dimorphisms were detected in those disorders[39,40]. Using PLS-MGA in schizophrenia we found significant differences between both women and men in the path from AOP to the phenomenome (quality of life) with a significant impact in women, but not in men[4]. On the other hand, no significant sex-related differences in the nomothetic network or in any of the pathways could be detected in mood disorders[3,5].

THE NOMOTHETIC MODEL AND THE REIFICATION OF DESCRIPTIVE ILLNESS NARRATIVES

In summary, a bottom-up, data-driven model of mood disorders and schizophrenia may be constructed using the knowledge-based causal framework shown in Figure 2 and by assembling R/R, AOPs, and phenome feature sets into an explicit data model, namely the PLS nomothetic network. Nomothetic indicates the tendency to generalize and to derive models ("laws") from independent variables, which explain variations in phenomena[41]. As such, the nomothetic network approach objectivates the symptomatome and phenomenome of mood disorders and schizophrenia[3-5], and, therefore, translates R/R, AOP, brainome, and cognitome feature sets into relevant descriptive narratives. The process which reifies the abstract concepts of descriptive narratives to realize a more concrete and material concept using computer science is named "reification of clinical diagnosis". It is important to note that in contrast to pan-omics and precision psychiatry, the aim of our nomothetic network approach is not only to compute pathways-phenotypes or biosignatures, but especially to make a nomothetic network, with causal links between the building blocks of the disease.

It should be added that this nomothetic network approach, in contrast to biological psychiatry models[42-44], may pass Karl Popper's critical rationalism test[33]. Indeed, our nomothetic networks are progressive (the model is based on all available knowledge), parsimonious (through feature reduction), changeable (other researchers can elaborate on the model and add more indicators or delete less robust features), provisional (the latent variable scores of the network will change when more pan-omics and brainome data are added), and falsifiable (the network can be refuted or corroborated). In this respect, our nomothetic networks deserve validation in more heterogeneous study groups consisting of individuals with comorbid psychiatric and medical disorders.

DISCOVERY OF NEW CLASSIFICATIONS BASED ON THE FEATURE SET SCORES

After integrating the validated feature vectors into a well-fitting nomothetic network, latent variable scores may be computed which reflect the severity of the various R/R, AOP, brainome, cognitome, staging, symptomatome, and phenomenome feature sets. The latter may be employed in unsupervised pattern recognition methods, including clustering analysis, to expose new categories (Figure 3). Previously, we employed different clustering techniques on such latent variable scores including K-mean, K-median, and Ward's and Forgy's methods[3-5]. Figure 4 shows a hypothetical example of cluster analysis-generated classes, with the latent variable scores (in z transformation) displayed in a clustered bar graph. This figure shows a normal cluster with healthy control subjects and two patients clusters. The second patient cluster may be discriminated from the first cluster (and from controls) by higher R/R, AOP, cognitive and brainome, symptomatome and phenomenome scores. The first patient cluster may be discriminated from controls by increased R/R3, AOP, and phenome scores. Previously, we showed that, in mood disorders, these new bottom-up cluster analysis-derived classes are more influential for classification purposes than the top-down classification into bipolar type 1 and type 2 and major depression. As such, new mechanistic, biosignature-based, and/or transdiagnostic classes may be discovered[3,5].

Nevertheless, these new classes should be cross-validated in independent samples using other machine learning methods including support vector machine with 10-fold cross-validation or soft independent modeling of class analogy (SIMCA)[7]. It is interesting to note that our nomothetic networks computed in mood disorders and schizophrenia contain self-rated phenomenological features (including self-rated quality of life and severity of disabilities), and, therefore, may comprise idiographic features[3,4]. Therefore, the latent variable scores not only delineate an objective nomothetic network and new diagnostic classes, but also shape an idiomatic feature profile, which is unique for every individual. As such, adequate treatments of mood disorders and schizophrenia should target the components of the nomothetic networks (R/R, AOP, brainome) constructed in those disorders. In addition, the individualized feature profile allows a more personalized treatment targeting aberrations in specific R/R, AOP, cognitome, brainome, and staging latent variable scores.

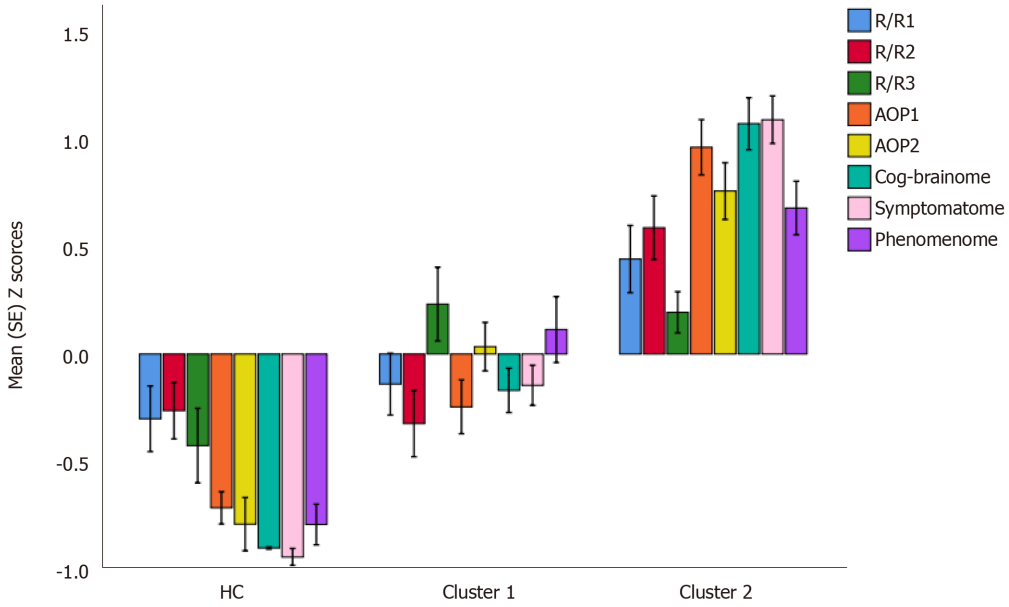

Figure 4 A hypothetical example of cluster analysis-generated classes, with the latent variable scores (in *z* transformation) displayed in a clustered bar graph. R/R: Risk/resilience; AOP: Adverse outcome pathway; HC: Healthy control.

CONCLUSION

In this paper we explained how to use the new nomothetic network psychiatry (NNP) approach to construct new causal models of mental illness by machine learning techniques, which assemble all features of mental illness, namely risk-resilience, AOPs, cognitome, brainome, symptomatome, staging, and phenomenome scores. PLS analysis may successfully be used to train, test and validate those models, to build pathway-phenotypes or biosignatures, and to construct comprehensive models of mood disorders and schizophrenia which objectivate the clinical phenome of those disorders. Clustering analysis performed on all illness features reduced into latent traits may expose relevant new (transdiagnostic) classes. The reification of the clinical diagnosis of mood disorders and schizophrenia (and by inference other psychiatric disorders) using the nomothetic network psychiatry approach is an awaited achievement which constitutes a major paradigm shift in psychiatry[16].

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ORIGINAL ARTICLE

Case Control Study

What gets in the way of social engagement in schizophrenia?

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Abstract

BACKGROUND

Social engagement-important for health and well-being-can be difficult for people with schizophrenia. Past research indicates that despite expressing interest in social interactions, people with schizophrenia report spending less time with others and feeling lonely. Social motivations and barriers may play an important role for understanding social engagement in schizophrenia.

AIM

To investigate how people with schizophrenia describe factors that impede and promote social engagement.

METHODS

We interviewed a community sample of people with (n = 35) and without (n = 27) schizophrenia or schizoaffective disorder about their social interactions with friends and family over the past week and planned social activities for the coming week. We reviewed the interview transcripts and developed a novel coding system to capture whether interactions occurred, who had initiated the contact, and frequency of reported social barriers (*i.e.*, internal, conflict-based, logistical) and social motivations (*i.e.*, instrumental, affiliative, obligation-based). We also assessed symptoms and functioning.

RESULTS

People with schizophrenia were less likely than people without schizophrenia to have spent time with friends [t (51.04) = 2.09, P = 0.042, d = 0.51)], but not family. People with schizophrenia reported more social barriers than people without schizophrenia [F (1, 60) = 10.55, P = 0.002, ηp2 = 0.15)] but did not differ in

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reported social motivations. Specifically, people with schizophrenia reported more internal [t (45.75) = 3.40, P = 0.001, d = 0.83)] and conflict-based [t (40.11) = 3.03, P = 0.004, d = 0.73)] barriers than people without schizophrenia. Social barriers and motivations were related to real-world social functioning for people with schizophrenia, such that more barriers were associated with more difficulty in close relationships (r = -0.37, P = 0.027) and more motivations were associated with better community functioning (r = 0.38, P = 0.024).

CONCLUSION
These findings highlight the importance of assessing first person accounts of social barriers and motivations to better understand social engagement in schizophrenia.

Key Words: Social engagement; Schizophrenia; Social motivation; Social barriers

Core Tip: We examined factors that may impede and promote social engagement in schizophrenia. We coded social barriers and motivations from transcribed negative symptoms interviews. We found that barriers, such as conflicts with other people or negative beliefs about the self, were prominent in schizophrenia. Interestingly, when explicitly prompted, people with schizophrenia reported interest in and motivation for social interactions. Nevertheless, social barriers may get in the way of them following through.

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INTRODUCTION

Social engagement is a central part of life and is linked to many benefits, such as wellbeing, health, and longevity[1]. Unfortunately, limited social engagement is common in schizophrenia[2] and people with schizophrenia often miss out on the benefits of such engagement. In this study, we sought to determine contributing factors to limited social engagement in schizophrenia. Specifically, we examined how people with and without schizophrenia talk about their social engagement with friends and family to better understand factors that motivate such engagement and barriers that might get in the way.

Why might people with schizophrenia engage in fewer social interactions? Limited social engagement may be indicative of social disinterest[3]. Indeed, people with schizophrenia report spending less time around others and set fewer social goals compared to people without schizophrenia[4-6]. However, other evidence indicates that people with schizophrenia describe social relationships as equally important[7,8] and express as much interest in social activity compared to people without schizophrenia[4,9]. Moreover, people with schizophrenia report a similar or even greater preference to be with others as those without schizophrenia when they find themselves alone[10,11]. People with schizophrenia also express more social interest than those with other psychiatric illnesses[12]. Even as people with schizophrenia profess an interest in social interactions, they also report feeling lonely[5,13-15], suggesting they have social needs that are not being met. Insofar as diminished interest does not fully account for limited social engagement in schizophrenia, we sought to examine other possible barriers. Understanding what might get in the way of social engagement in schizophrenia can be an important first step toward helping people with schizophrenia obtain the myriad benefits of social interactions.

Social barriers

Barriers that may interfere with social engagement in schizophrenia include internal

states, conflicts with others, or logistical factors. Prior research has identified several possible internal barriers in schizophrenia, including low self-esteem, internalized stigma, and defeatist performance beliefs[16-19]. Symptoms may also interfere with social engagement: Greater positive symptoms are associated with lower relationship satisfaction[20], and greater negative symptoms are associated with smaller social network sizes[21,22].

Conflicts with others, whether in the form of disagreements, social discrimination, or stigma-related rejection, may also interfere with social engagement. For example, families with a person with schizophrenia report more frequent arguments and heightened tension than other families[23]. People with schizophrenia are often reluctant to disclose their illness to friends, fearing that once they do, they will be rejected[24].

Logistical barriers, such as limited financial means, may also get in the way of social engagement. People with schizophrenia are more likely to be unemployed[25], which could restrict social network size and variety[26]. Social activities that require money or transportation may also be less accessible[27].

Social motivations

Considering what motivates people to form and maintain relationships is also important for understanding social engagement. Some motivations for relationships are instrumental, arising from a desire for social activity to acquire tangible benefits[28,29]. In this way, relationships are a means to an end. As caregivers of people with schizophrenia are at times responsible for meeting various needs of their loved ones[30], the desire for assistance may be a motivation for social engagement.

Alternatively, social relationships can be motivating in and of themselves[29,31]. Affiliative motivations focus on companionship, mutual care, and the exchange of emotions as drivers of engagement with others. People with schizophrenia report wanting social relationships and even consider them a primary source of meaning[32], suggesting that affiliative motivations are an important aspect of social engagement. Another type of social motivation is obligation-based, which refers to the desire to meet personally or societally determined standards of appropriate social behavior[33], or how a person "should" behave. Because it is considered normative to have relationships, people with schizophrenia report this as an important indication of health[34].

The importance of first-person accounts

How people with schizophrenia describe their social experiences can offer a window into social barriers and motivations and provide an important perspective for understanding social engagement. Of the few studies in schizophrenia that have used such an approach, most have focused on lexical characteristics of speech, linguistic abnormalities, word counts, or speech coherence and appropriateness[35-40]. A notable exception is the work of Lysaker *et al*[41], who assessed social worth, social closeness, and personal agency in spoken narratives of people with schizophrenia. The more frequently people with schizophrenia referred to these social themes in their narratives, the better their social functioning.

Present study

We sought to answer four questions about social engagement in schizophrenia. First, we asked whether people with and without schizophrenia differed in the frequency and initiation of interactions with family and friends in the past week. Second, we asked whether people with and without schizophrenia differed in reported types of social barriers and motivations. Third, we asked whether social barriers and motivations differed by relationship type (friends, family). Fourth, we asked whether social barriers and motivations were related to functioning and symptoms for people with schizophrenia.

MATERIALS AND METHODS

Participants

Thirty-five people with schizophrenia (n = 26) or schizoaffective disorder (n = 9) and 27 people without a schizophrenia spectrum disorder participated. People with schizophrenia and schizoaffective disorder did not differ from one another on any demographic, clinical, or coded variable; we collapsed across these groups for

analyses. Participants were recruited from board and care homes, nonprofit agencies, and Craigslist and were part of the multi-site study that developed the Clinical Assessment Interview for Negative Symptoms[42]. The data presented here do not overlap with that study.

Diagnoses were confirmed using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I/P)[43]. For controls, we administered the SCID non-patient version (SCID-I/NP)[44] to confirm absence of schizophrenia spectrum disorders. Any participant with a history of head injury or neurological disorder, a current mood episode, or substance use disorder within the past six months was not invited to participate. All participants provided written informed consent. As shown in Table 1, the groups did not differ in age, sex, race, marital status, education, or estimated intelligence quotient (measured by the Wechsler Test of Adult Reading[45]).

Measures

Clinical Assessment Interview for Negative Symptoms beta version: Trained raters administered the beta version of the Clinical Assessment Interview for Negative Symptoms (CAINS), and the interviews were videotaped. The CAINS includes several manualized open-ended probes for each item with additional questions asked as needed for clarity. The CAINS-beta differs from the final CAINS[46] in length (16 rather than 13 items) and in the inclusion of separate questions about romantic relationships.

We examined responses to the first five items of the CAINS-beta. The first three items assessed social motivation and enjoyment in (1) family; (2) romantic relationships; and (3) friendships. Participants were asked to describe their social interactions over the preceding week (*e.g.*, Have you been motivated to be around or in touch with your family/partner/friends in the past week?). The fourth item asked participants to describe pleasure experienced in past week social activities (*e.g.*, Did you have any enjoyable interactions with other people?), and the fifth item asked about expected pleasure from social activities over the next week (*e.g.*, What do you think you will enjoy doing in the next week with other people?).

Interview coding: Interviews were transcribed and coded by trained research assistants. We developed a coding manual containing definitions and examples for all variables, and four raters, blind to diagnostic status, did the coding. A different rater reviewed all data for entry accuracy and coding manual adherence.

Mirroring the final CAINS[46], marital relationships were included with family items, and dating relationships were included with friend items. For friends and family, coders rated "whether any interaction had occurred" over the past week—including phone calls, text messages, e-mails, or in-person contact—dichotomously (present, absent). When an interaction was reported, "initiation" was coded on a 3-point scale: (1) Social partner(s) initiated all interactions; (2) Participant initiated some and social partner initiated some; and (3) Participant initiated all interactions.

Coders determined which type of social barrier or motivation a statement referred to and then computed the total number of social barriers and motivations of each type. Social barriers were defined as causing an interaction to be cut short or to not occur at all. Coders counted the frequencies of three types of barriers. Internal barriers included psychological states and beliefs that prevented interaction, including negative self-perceptions or self-stigma (*e.g.*, "No one would want to be my friend"), psychiatric symptoms, negative beliefs about social interactions (*e.g.*, "People just let you down"), and having goals or priorities that took precedence over social interaction (*e.g.*, "I want to finish my degree before I look for a relationship"). Conflict-based barriers included discrimination (*e.g.*, "My parents disowned me because I'm gay"), rejection (*e.g.*, "She said she didn't want to date anymore"), and social conflict (*e.g.*, "All we ever do is fight"). Logistical barriers referred to geographic distance, lack of time, mismatched schedules, non-psychiatric illness, lack of financial resources, or perceived lack of access to an appropriate social partner.

Coders also computed the frequencies of three types of social motivations. Instrumental motivations included tangible benefits (*e.g.*, a relative paying for rent) and perceived benefits to a participant's physical or mental wellbeing or personal development (*e.g.*, "She keeps me sane"). Affiliative motivations included positive attributes of interaction partners (*e.g.*, "He's funny"), social support, acceptance of self (*e.g.*, "I feel like I can be myself around them"), physical intimacy, and avoidance of loneliness and social isolation. Obligation-based motivations included a desire to provide something to an interaction partner (*e.g.*, "I want to be a positive role model for my sister"), or expectations of normative behavior (*e.g.*, "I called my friend on her birthday because it is the polite thing to do"). Finally, we counted the total number of words participants uttered using the Linguistic Inquiry and Word Count program[47].

Table 1 Demographic and clinical characteristics

	Schizophrenia	Control
Age (in year)	45.20 (10.96)	45.11 (8.51)
Sex, *n* (%)	12 Female (34.3)	10 Female (37.0)
Race, *n* (%)		
White	18 (51.4)	8 (29.6)
Black	9 (25.7)	10 (37.0)
Asian	2 (5.7)	3 (11.1)
Pacific Islander	1 (2.9)	0 (0)
Multiracial	2 (5.7)	15 (8.5)
Ethnicity: Hispanic/Latino, *n* (%)	3 (8.6)	4 (14.8)
Education (in year)	14.32 (2.80)	14.96 (2.79)
Employed, *n* (%)	16 (45.7)	15 (55.6)
Marital status		
Married	14.3%	29.6%
Widowed	2.9%	0%
Divorced/Separated	17.1%	22.2%
Never married	65.7%	44.4%
Unknown	0%	3.7%
Percent employed	45.7%	55.6%
WTAR	104.12 (15.18)	102.67 (12.45)
Diagnosis	Schizophrenia: 74.3%	--
	Schizoaffective: 25.7%	
Duration of illness (in year)	22.52 (12.42)	--
BPRS	46.03 (11.81)	--
RFS		
Working productivity	4.43 (2.12)	--
Independent living skills	5.37 (1.57)	--
Immediate social network	5.20 (1.62)	--
Extended social network	4.37 (1.94)	--
CAINS-EXP	1.21 (0.82)	0.56 (0.59)
CAINS-MAP[a]	1.87 (0.71)	1.00 (0.68)

Values are means with standard deviations in parentheses or numbers with percentages.
[a]Mean of 13 items from the final Clinical Assessment Interview for Negative Symptoms and romantic relationship motivation item from Clinical Assessment Interview for Negative Symptoms-beta. BPRS: Brief Psychiatric Rating Scale; CAINS-EXP: Clinical Assessment Interview for Negative Symptoms, Expression Subscale; CAINS-MAP: Clinical Assessment Interview for Negative Symptoms, Motivation and Pleasure Subscale; RFS: Role Functioning Scale; WTAR: Wechsler Test of Adult Reading.

Clinical ratings: We measured functioning using the Role Functioning Scale[48] with its 1 (minimal functioning) to 7 (optimal functioning) point scale. The Role Functioning Scale contains four subscales—working productivity, independent living and self-care, immediate social network relationships, and extended social network relationships. We assessed symptoms using a 24-item version of the Brief Psychiatric Rating Scale rated on a 7-point scale[49].

Data analyses

We conducted independent samples *t*-tests and chi-square tests to compare demographics, word count, contact, and initiation. For barriers and motivations, we conducted 2 Group (schizophrenia, control) X 2 Relationship Type (family, friends) X 3 Barrier (internal, logistical, conflict-based) or Motivation Type (instrumental, affiliative, obligation-based) mixed effect analyses of variance. Sphericity violations were Greenhouse-Geisser corrected; effect sizes are reported as Cohen's d and partial eta squared (ηp2). We computed Pearson correlations between barriers, motivations, functioning, and symptoms within the schizophrenia group.

RESULTS

Preliminary analyses

Two coders rated a third of interviews (equal numbers of people with and without schizophrenia) to assess inter-rater agreement. Coders achieved a high rate of agreement, with intraclass correlations[50] ranging from 0.83-1.00.

People with (M = 1652.66, SD = 958.25) and without (M = 1348.08, SD = 926.58) schizophrenia did not differ significantly in the amount of words spoken during the interview [t (59) = 1.25, P = 0.22, d = 0.32)]. Thus, any group differences in coded barriers and motivations were not a function of fewer words uttered by either group. We also found no significant differences between men and women for any variable, and thus we collapsed across sex for subsequent analyses.

Contact and initiation

Both groups were just as likely to have interacted with family over the past week, but people with schizophrenia were less likely to have interacted with friends compared to controls, [t (51.04) = 2.09, P = 0.042, d = 0.51]. People with schizophrenia were no more likely to be living with family than those without schizophrenia [t (59) = -0.96, P = 0.34, d = 0.25)], suggesting that greater ease of access did not contribute to rates of reported family interactions for the schizophrenia group. When interactions did occur, the groups were equally likely to have initiated interactions with family. However, people with schizophrenia were less likely to have initiated interactions with friends, [t (46) = 2.75, P = 0.008, d = 0.80].

Barriers

We found a significant group main effect [F (1, 60) = 10.55, P = 0.002, ηp2 = 0.15)], indicating that people with schizophrenia reported more barriers overall than people without schizophrenia (see Table 2). However, the Group X Barrier Type interaction was also significant [F (2, 120) = 3.27, P = 0.041, ηp2 = 0.05)], indicating that the group differences depended upon barrier type. As shown in Figure 1, people with schizophrenia reported more internal [t (45.75) = 3.40, P = 0.001, d = 0.83) and conflict-based barriers [t (40.11) = 3.03, P = 0.004, d = 0.73)] than people without schizophrenia; the groups did not differ in reported logistical barriers.

We also found a significant relationship type main effect [F (1, 60) = 10.35, P = 0.002, ηp2 = 0.15)], indicating that all participants reported more barriers for friends than family [t (61) = 3.36, P = 0.001, d = 0.43)]. However, this was qualified by a significant Relationship Type X Barrier Type interaction [F (2, 120) = 3.78, P = 0.026, ηp2 = 0.06)]. As shown in Table 3, whereas logistical and conflict-based barriers were similar across friends and family, all participants reported more internal barriers for friends than for family [t (61) = 4.10, P < 0.001, d = 0.52)].

Motivations

Neither the group main effect [F (1, 60) = 0.17, P = 0.68, ηp2 = 0.003)], nor the Group X Motivation Type interaction were significant [F (1, 60) = 1.92, P = 0.17, ηp2 = 0.03)]. However, the motivation type main effect was significant [F (1.10, 65.89) = 143.42, P < 0.001, ηp2 = 0.71)]; all participants reported more affiliative than instrumental [t (61) = 12.07, P < 0.001, d = 1.53)] or obligation-based [t (61) = 8.36, P < 0.001, d = 1.06)] motivations (see Table 2). In addition, participants reported more obligation-based than instrumental motivations [t (61) = 4.14, P < 0.001, d = 0.53)].

This finding was qualified by a significant Relationship Type X Motivation Type interaction [F (1.19, 71.41) = 4.14, P = 0.039, ηp2 = 0.07)]. Whereas obligation-based motivations were similar across friends and family, all participants reported more instrumental [t (61) = 2.02, P = 0.048, d = 0.26)] and affiliative motivations [t (61) = 2.14,

Table 2 Contact, initiation, barriers, and motivations by group

	Schizophrenia	Control	*P* value	Cohen's *d*
Contact	1.84 (0.23)	1.93 (0.18)	0.09	0.43
Initiation	1.75 (0.66)	2.03 (0.66)	0.11	0.42
Barriers				
Internal	2.00 (2.28)	0.57 (0.86)	0.001	0.83
Logistical	1.57 (1.26)	1.43 (1.46)	0.68	0.11
Conflict-based	1.53 (2.40)	0.24 (0.64)	0.004	0.73
Motivations				
Instrumental	0.90 (1.10)	0.69 (0.91)	0.41	0.21
Affiliative	8.27(5.67)	8.98 (4.15)	0.59	0.14
Obligation-based	3.09 (4.57)	3.39 (4.06)	0.79	0.07

Values are means with standard deviations in parentheses.

Table 3 Barriers and motivations by relationship status

	Friends	Family	*P* value	Cohen's *d*
Barriers				
Internal	1.09 (1.60)	0.29 (0.69)	0.001	0.52
Logistical	0.85 (1.02)	0.65 (0.91)	0.26	0.15
Conflict-based	0.52 (1.55)	0.44 (0.81)	0.68	0.05
Motivations				
Instrumental	0.51 (0.67)	0.30 (0.64)	0.048	0.26
Affiliative	4.82 (3.25)	3.76 (3.05)	0.037	0.28
Obligation-based	0.38 (0.66)	0.55 (0.78)	0.23	0.15

Values are means with standard deviations in parentheses.

$P = 0.037$, $d = 0.28$)] for friends than for family.

Correlations

As shown in Table 4, barriers and motivations were significantly associated with functioning. Internal and conflict-based barriers were moderately, negatively correlated with independent living skills, indicating that the more difficulties people with schizophrenia experienced with self-care, the greater the number of internal and conflict-based barriers they reported. More logistical barriers were associated with greater difficulties with close others. Motivations were moderately related to social functioning; in particular, more affiliative motivations were associated with significantly better social functioning within the broader community.

Interestingly, only conflict-based barriers were significantly related to total symptoms (but not negative or positive symptoms separately), suggesting that other types of barriers/motivations may be somewhat independent of symptom severity.

DISCUSSION

We investigated reported barriers to and motivations for social engagement in people with and without schizophrenia. Despite describing social engagement with the same number of words, people with schizophrenia reported more social barriers than those without schizophrenia, yet just as many social motivations. Importantly, social barriers and motivations were also related to functioning. Our findings suggest that particular

Table 4 Correlations with functioning and symptoms

	Barriers			Motivations		
	Internal	Logistical	Conflict-based	Instrumental	Affiliative	Obligation-based
Role Functioning Scale						
Working productivity	0.03	0.13	-0.20	-0.01	0.23	0.06
Independent living/self-care	-0.36[a]	0.02	-0.43[b]	-0.08	-0.26	-0.22
Immediate social network	-0.16	-0.37[a]	-0.18	-0.08	0.01	-0.16
Extended social network	-0.18	0.12	-0.20	-0.10	0.38[a]	0.22
BPRS	0.25	-0.14	0.50[b]	0.20	-0.03	-0.001

[a]$P < 0.05$.
[b]$P < 0.01$. BPRS: Brief Psychiatric Rating scale.

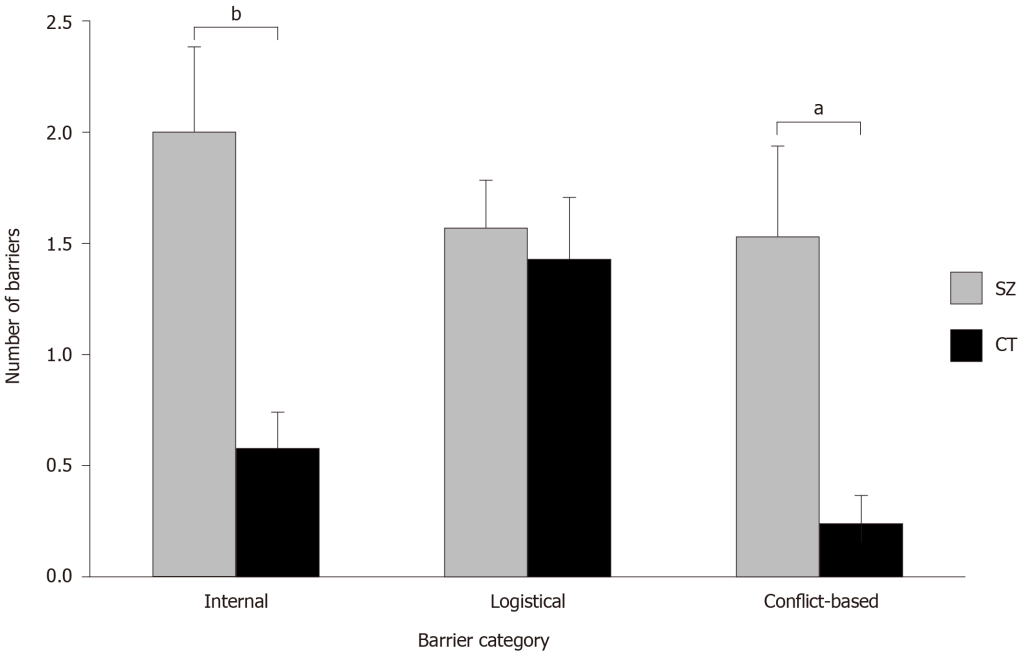

Figure 1 Barriers reported (collapsed across relationship type) for people with (SZ) and without (CT) schizophrenia. People with schizophrenia reported significantly more barriers than controls, in general, as well as more internal and conflict-based barriers specifically. [a]$P < 0.01$ and [b]$P < 0.001$. SZ: Schizophrenia; CT: Computed tomography.

types of social barriers and motivations may impede social engagement for people with schizophrenia and impact real-world social behavior, and they provide valuable information on directions for improving social engagement.

Consistent with previous research[51], we found that people with schizophrenia were less likely to have interacted with or initiated contact with friends over the past week compared to controls. However, we found no differences in contact or initiation with family. These findings are clinically important, as frequency of contact with friends is more predictive of clinical recovery than contact with family[52]. Moreover, evidence suggests that people with schizophrenia lose connections with close friends early in the course of illness[51], which may contribute to limited social engagement over the illness course[53].

Compared to controls, people with schizophrenia reported experiencing more internal barriers and conflict-based barriers. These findings are consistent with evidence that people with psychotic disorders feel less at ease and more threatened while in the company of others compared to people without psychotic disorders[11]. It is possible that people with schizophrenia are more sensitive to perceiving negativity in social encounters; however, it is also possible that negative attitudes are borne from actual social rejection.

Although speculative, conflict-based barriers may be associated with stigma-based rejection. Heightened discrimination and rejection that people with schizophrenia face may perpetuate negative beliefs about social interactions, resulting in a cycle of negative social experiences. It would be helpful for future work to explore the origins and bidirectional causality of conflicts involving people with schizophrenia. Impairments in social cognitive processes (*e.g.*, social cue perception, empathy), which we did not assess, could make resolving disagreements more challenging for people with schizophrenia[54]. Examining linkages between social barriers and stigma-based rejection is an important direction for future research.

Both groups reported more barriers to interactions with friends than with family, and this was particularly evident for internal barriers. Friendships are inherently more difficult since they are not "built in" and thus require more effort to establish and maintain. Family members may reach out frequently even if their loved one has negative beliefs about interactions. By contrast, friends may not put in this effort. Coupled with our finding that people with schizophrenia were less likely to interact with friends and also that barriers were more common for interactions with friends, it seems especially important to study friendships in future studies.

Interestingly, we found that people with schizophrenia reported being comparably motivated for friend and family interactions as people without schizophrenia. This finding may seem at odds with other studies indicating that people with schizophrenia have deficits in social motivation[55-57]. Two methodological differences may account for this discrepancy. First, similar to Gard *et al*[4], we asked people to report on their actual, "real-life" social interactions over the past week following several guided prompts. By contrast, laboratory studies of social motivation use tasks of simulated social interactions. Second, we coded actual behavior (*e.g.*, went to dinner with family) as well as articulated motives (*e.g.*, reported desire to see family). This approach differs from studies of effort expenditure[56,58] that focus on behavioral action. It will be informative in future studies to examine social motivations using a variety of approaches, such as ecological momentary assessment, passive mobile data collection, or virtual reality techniques[59]. Moreover, it will be essential to replicate this finding with a larger sample, as social motivation difficulties, like any deficit in schizophrenia, are not observed in all people with the diagnosis.

We found that both groups reported more affiliative and instrumental motivations for friendships than family relationships, which is noteworthy since people with schizophrenia were less likely to have had contact with friends. That is, people with schizophrenia reported being motivated to interact with friends for affiliative and instrumental reasons as much as controls, yet they were less likely to have done so over the past week. This finding highlights an important disconnect between reported interest and actual behavior for people with schizophrenia[59-61]. Although experiencing motivation for friendships may provide entry to important support that comes from friendships[62-65], receipt likely requires contact with friends. Understanding how internal or conflict-based social barriers can be reduced will likely help increase contact and benefits from friends.

We also found that barriers and motivations were associated with real-world functioning for people with schizophrenia. Because navigating the social world is important for autonomous living, conflict-based barriers, such as stigma and rejection, may make it more challenging for people with schizophrenia to maneuver bureaucratic systems or manage shopping or transportation. Similarly, internal barriers, like negative beliefs about the self, may be detrimental to the self-efficacy necessary to pursue independent living[66].

Encouragingly, we found no group differences in reported logistical barriers, perhaps because the groups did not differ in education or employment status. Nevertheless, for people with schizophrenia, logistical barriers were associated with functioning in close relationships. Although finances are but one type of logistical barrier, limited means can make it more difficult for people with schizophrenia to afford social activities or access transportation. Relatedly, unemployment[25] or lessened community integration[67] may make it challenging to get in touch with or visit other people.

The more that people with schizophrenia were motivated by the interpersonal aspects of relationships, the better their functioning in wider spheres of social contact such as clubs, churches, or social recreational activities. Perhaps people who value the relational aspects of social interactions seek out more opportunities for contact with members of their communities. Given the cross-sectional and correlational nature of our data, however, it is impossible to assess directionality. Nevertheless, social integration in different spheres is an important predictor of quality of life[18].

Fortunately, many of the barriers that we have identified are already the targets of

current treatments. For example, internal barriers, such as negative beliefs about relationships, have been targeted in Cognitive Behavioral Therapy for negative symptoms. Cognitive Behavioral Social Skills Training's[68,69] emphasis on communication and assertiveness skills and family therapy's focus on problem solving may assist with conflict-based barriers[70].

Although these findings provide an important step towards understanding what hinders and helps people with schizophrenia build social engagement, they should be considered in the context of limitations. First, our assessment of barriers and motivations was limited to participants' responses to the CAINS. Because specific barriers or motivations were not asked about explicitly, we may have undercounted, and we may not have captured all types of barriers (*e.g.*, social anxiety). Nevertheless, the CAINS includes more questions about social interactions than most clinical interviews, and thus the corpus of reported social engagement was richer than it might have been with a different interview.

Second, although we assessed the presence of barriers and motivations, we did not assess their relative contributions to impeding social engagement. For instance, although geographic distance (logistical barrier) and negative beliefs (internal barrier) may have been reported, it is possible that the negative beliefs were more impeding than distance. Third, the CAINS assessed the preceding and upcoming week, thus limiting the time period for reporting on social engagement. On the other hand, the strength of this approach is that it reduced difficulties and biases associated with retrospective reports. Fourth, all participants were taking antipsychotic medication so we cannot ascertain what, if any, impact medications may have had on participant responses. Finally, we did not assess related constructs, such as social network size, and thus future studies would benefit from investigating these alongside motivations and barriers to better understand the relationships between them.

CONCLUSION

In summary, we found that people with schizophrenia were less likely to interact with and initiate contact with friends compared to people without schizophrenia even as they did not differ in contact with family. Our findings suggest that certain types of social barriers get in the way of social engagement in schizophrenia, including barriers involving the self and conflicts with others. Importantly, social barriers and motivations were also related to real world functioning, suggesting that asking people to describe their social lives is linked to independent assessments of functioning. Together, our approach illustrates the benefits of simply asking people to describe their social lives and suggests that efforts to help mitigate social barriers might improve social engagement.

ARTICLE HIGHLIGHTS

Research background

Though limited social engagement is common in schizophrenia, the reasons for this remain unclear. People with schizophrenia report a desire to be with others, and yet spend more time alone.

Research motivation

Better understanding of the factors that contribute to limited social engagement can be an important first step toward helping people with schizophrenia to meet their social needs.

Research objectives

To identify and compare motivations and barriers for social engagement with friends and family among those with and without schizophrenia.

Research methods

Thirty-five people with schizophrenia or schizoaffective disorder and 27 nonclinical controls were recruited from the community to participate in this study. Participants completed measures of symptoms and functioning, as well as a negative symptoms interview, which asked participants to describe their engagement in and motivation

for social activities in the past and upcoming weeks. Using a novel coding system, we coded the frequency with which participants described six types of social motivations and barriers.

Research results

People with schizophrenia were less likely to interact with and initiate contact with friends, but not family, compared to nonclinical controls. The groups differed in reported barriers, such that people with schizophrenia reported more internal and conflict-based barriers than those without schizophrenia. People with and without schizophrenia reported similar numbers and types of motivations for social engagement. Barriers and motivations were associated with symptoms and functioning.

Research conclusions

This study suggests that barriers, such as conflicts with other people or negative beliefs about the self may interfere with social engagement in schizophrenia. People with schizophrenia report interest and motivation for social interactions, but social barriers may get in the way of them following through.

Research perspectives

Further exploration of social barriers in terms of types, frequency, and relative contribution to limiting social engagement is warranted.

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